


**CLAIM AMENDMENTS**

1. (currently amended): A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein

 represents a single or double bond;

each Z<sup>2</sup> is independently CR<sup>1</sup> or C(R<sup>1</sup>)<sub>2</sub> wherein ~~[[each]] one R<sup>1</sup> is independently hydrogen or noninterfering substituent~~ COCOR<sup>2</sup> and the remaining R<sup>1</sup>(s) are H;

wherein R<sup>2</sup> is H, or is straight or branched chain alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroaryl, or heteroarylalkyl, each optionally substituted with halo, alkyl, heteroalkyl, SR, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, CN, COOR, CONR<sub>2</sub>, COR, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl, or

wherein R<sup>2</sup> is OR, NR<sub>2</sub>, SR, NRCONR<sub>2</sub>, OCONR<sub>2</sub>, or NRSO<sub>2</sub>NR<sub>2</sub>, wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl, and wherein two R attached to the same atom may form a 3-8 member ring and wherein said ring may further be substituted by alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroalkyl, heteroalkenyl, heteroaryl, heteroarylalkyl, or optionally substituted with halo, SR, OR, NR<sub>2</sub>, OCOR, NRCOR, NRCONR<sub>2</sub>, NRSO<sub>2</sub>R, NRSO<sub>2</sub>NR<sub>2</sub>, OCONR<sub>2</sub>, or R<sub>3</sub>Si wherein each R is independently H, alkyl, alkenyl or aryl wherein two R attached to the same atom may form a 3-8 member ring, optionally substituted as above defined;

Z<sup>3</sup> is NR<sup>7</sup>, O, or S;

R<sup>7</sup> is hydrogen or a non-interfering substituent is optionally substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, or is SOR, SO<sub>2</sub>R, RCO, COOR, alkyl-COR, SO<sub>2</sub>R, CONR<sub>2</sub>, SO<sub>2</sub>NR<sub>2</sub>, CN, CF<sub>3</sub>, NR<sub>2</sub>, OR, alkyl-SR, alkyl-SOR, alkyl-SO<sub>2</sub>R, alkyl-OCOR, alkyl-COOR, alkyl-CN, alkyl-CONR<sub>2</sub>,

or  $R_3Si$ , wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl;

one of  $Z^4$  and  $Z^5$  is N and the other of  $Z^4$  and  $Z^5$  is  $CR^4$ , wherein  $R^4$  is as defined above CH; each  $R^3$  is independently a noninterfering substituent halo, alkyl, heteroalkyl, OCOR, OR, NRCOR, SR, or  $NR_2$ , wherein R is H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl;

n is 0-3;

each of  $L^1$  and  $L^2$  is a linker;

each  $R^4$  is independently a noninterfering substituent selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR,  $NR_2$ , SR, SOR,  $SO_2R$ , OCOR, NRCOR,  $NRCONR_2$ ,  $NRCOOR$ ,  $OCONR_2$ , RCO, COOR, alkyl-OOR,  $SO_2R$ ,  $CONR_2$ ,  $SO_2NR_2$ ,  $NRSO_2NR_2$ , CN,  $CF_3$ ,  $R_3Si$ , and  $NO_2$ , wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl, or  $R^4$  is  $=O$  or an oxime, oximeether, oximeester or ketal thereof;

m is 0-4;

$Z^1$  is  $CR^5$  or N wherein  $R^5$  is hydrogen or a noninterfering substituent H, OR,  $NR_2$ , SR or halo, wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl;

each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3; and

A is a cyclic group substituted with 0-5 noninterfering substituents, wherein two said noninterfering substituents can form a fused ring optionally substituted with 0-5 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR,  $NR_2$ , SR, SOR,  $SO_2R$ , OCOR, NRCOR,  $NRCONR_2$ ,  $NRCOOR$ ,  $OCONR_2$ , RCO, COOR, alkyl-OOR,  $SO_2R$ ,  $CONR_2$ ,  $SO_2NR_2$ ,  $NRSO_2NR_2$ , CN,  $CF_3$ ,  $R_3Si$ , and  $NO_2$ , wherein each R is independently H, alkyl, alkenyl, aryl, heteroalkyl, heteroalkenyl, heteroaryl or heteroarylalkyl.

2-5. (canceled)

6. (currently amended): The compound of ~~claim 5~~ claim 1 wherein  $R^7$  is H, or is optionally substituted alkyl, optionally substituted acyl, OR, or  $NR_2$  wherein each R is independently H, alkyl, alkenyl or aryl ~~or heteroforms thereof~~.

7. (original): The compound of claim 1 wherein both k and l are 1.

8. (original): The compound of claim 1 wherein  $L^1$  is CO, CHOH or  $CH_2$ .

9. (original): The compound of claim 8 wherein  $L^1$  is CO.

10. (original): The compound of claim 1 wherein  $Z^1$  is N.

11. (canceled)

12. (currently amended): The compound of claim 1 wherein  $L^2$  is alkylene (1-4C) or alkenylene (1-4C) optionally substituted with a moiety selected from the group consisting of alkyl, alkenyl, alkynyl, aryl, arylalkyl, acyl, aroyl, heteroaryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heteroalkylaryl, NH-aroyl, halo, OR,  $NR_2$ , SR, SOR,  $SO_2R$ , OCOR, NRCOR,  $NRCONR_2$ ,  $NRCOOR$ ,  $OCONR_2$ , RCO, COOR, alkyl-OOR,  $SO_3R$ ,  $CONR_2$ ,  $SO_2NR_2$ ,  $NRSO_2NR_2$ , CN,  $CF_3$ ,  $R_3Si$ , and  $NO_2$ , wherein each R is independently H, alkyl, alkenyl or aryl ~~or heteroforms thereof~~, and wherein two substituents on  $L^2$  can be joined to form a non-aromatic saturated or unsaturated ring that includes 0-3 heteroatoms which are O, S and/or N and which contains 3 to 8 members or said two substituents can be joined to form a carbonyl moiety or an oxime, oximeether, oximeester or ketal of said carbonyl moiety.

13. (original): The compound of claim 12 wherein  $L^2$  is unsubstituted alkylene.

14. (original): The compound of claim 13 wherein  $L^2$  is unsubstituted methylene.

15. (canceled)

16. (currently amended): The compound of ~~claim 15~~ claim 1 wherein A is optionally substituted phenyl.

17. (original): The compound of claim 16 wherein said optional substitution is by halo, OR, or alkyl.

18. (original): The compound of claim 17 wherein said phenyl is unsubstituted or has a single substituent.

19. (canceled)

20. (currently amended): The compound of ~~claim 19~~ claim 1 wherein each  $R^4$  is halo, OR, or alkyl.


21. (original): The compound of claim 20 wherein m is 0, 1, or 2.

22. (original): The compound of claim 21 wherein m is 2 and both  $R^4$  are alkyl.

23. (canceled)

24. (currently amended): The compound of ~~claim 23~~ claim 1 wherein  $R^3$  is halo or alkoxy.

25-27. (canceled)

28. (original): The compound of claim 1 wherein  represents a double bond.

29. (currently amended): The compound of claim 1 wherein  $Z^4$  is N and  $Z^5$  is  $\text{CR}^3\text{CH}$ .

30. (currently amended): The compound of claim 1 wherein  $Z^5$  is N and  $Z^4$  is  $\text{CR}^3\text{CH}$ .

31-32. (canceled)

33. (original): A pharmaceutical composition for treating conditions characterized by enhanced p38- $\alpha$  activity which composition comprises  
a therapeutically effective amount of at least one compound of claim 1 and at least one pharmaceutically acceptable excipient.

34-35. (canceled)

36. (withdrawn; currently amended): A method to treat a condition mediated by p38 kinase comprising administering to a subject in need of such treatment a compound of claim 1, or a pharmaceutical composition thereof wherein said condition is a proinflammation response.

37. (canceled)

38. (withdrawn; currently amended): The method of ~~claim 37~~ claim 36 wherein said proinflammation response is multiple sclerosis, IBD, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, other arthritic conditions, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, asthma, adult respiratory distress syndrome, stroke, reperfusion injury, CNS injury, psoriasis, restenosis, cerebral malaria, chronic pulmonary inflammatory disease, chronic obstructive pulmonary disease, cystic fibrosis, silicosis, pulmonary sarcosis, bone fracture healing, a bone resorption disease, soft tissue damage, graft-versus-host reaction, Crohn's Disease, ulcerative colitis, Alzheimer's disease or pyresis.

39. (currently amended): ~~[[The]] A compound of claim 1 wherein the compound of formula (1) is selected from the group consisting of the title compounds made in of Examples 1-27, 10 and the additional compounds of Examples 11 and 23.~~

40-41. (canceled)

42. (new) A compound selected from the group consisting of the title compound of Example 12 and the additional compounds of Examples 13 and 24.

43. (new) A compound selected from the group consisting of the title compound of Example 14 and the additional compounds of Examples 15 and 25.

44. (new) A compound selected from the group consisting of the title compounds of Examples 16-22 and the additional compounds of Example 23.

45. (new) A compound selected from the group consisting of the title compounds of Examples 26-36 and the additional compounds of Example 37.